UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,832	03/28/2002	Takeshi Nagasu	082370-000000US	8651

7590 10/31/2003

Joe Liebeschuetz
Townsend & Townsend & Crew
8th Floor
Two Embarcadero Center
San Francisco, CA 94111-3834

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,832	NAGASU ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☒ Claim(s) *3-9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) ~~Paper No(s).~~ filed 6/9/03 & 10/21/02
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I, claims 1-9 in the paper received 8/18/03 is acknowledged.

2. Claims 1-9 are examined herein, claims 10-20 are withdrawn as being non-elected.

3. Prior to entry into the PTO STIC database, the computer readable form of the sequence listing was corrected by the deletion of non-ASCII "garbage" at the beginning/end of files.

4. The change in the title requested by applicant in the paper received 7/8/02 is approved by the examiner. The request to change the title in the PTO database will be forwarded to the appropriate support staff.

Claim Objections

5. Claims 3-9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 is broader in scope than claim 1 and does not require all of the limitations of claim 1. For example, fragments of instant SEQ ID NO: 1 would specifically hybridize to the nucleic acid molecule of claim 1. These fragments would not, therefore, comprise SEQ ID NO: 1, as is required by claim 1. Therefore claim 3 is improperly dependent because instead of limiting claim 1, it expands the scope of claim 1. Further, claims 4-9 are all method claims which depend from claim 1 but do not include all of the limitations of claim 1 and are therefore not properly dependent from claim 1 because they require only nucleic

acids that hybridize to the sequence of claim 1 which is a broader recitation than the nucleic acid comprising SEQ ID NO: 1.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a nucleic acid molecule **comprising** the nucleotide sequence of SEQ ID NO: 1. Instant SEQ ID NO: 1 is a partial cDNA molecule which is demonstrated in the specification as being useful for detecting a predisposition to cedar pollen allergy. The specification teaches that a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 "includes the full length gene 513 cDNA which can be isolated... (specification, page 8, lines 31-34)." The specification does not provide written description of the full length gene 513 cDNA. Furthermore, depending on the portion of the full length cDNA that SEQ ID NO: 1 represents, this claim also encompasses a full length genomic DNA (i.e. if it is only a portion of a single exon), nucleic acids encoding fusion proteins, splice variants of the full length cDNA, etc.

Claim 2 is drawn to a nucleic acid molecule comprising the coding region of the nucleotide sequence of SEQ ID NO: 1. Like claim 1, this molecule would include the full length

cDNA of which SEQ ID NO: 1 is a fragment. Further, the claim specifically denotes the "coding region" but the specification does not describe which portion of SEQ ID NO: 1 is a "coding region" as opposed to untranslated portions of the partial cDNA. Since the cDNA is a partial cDNA, it is not possible to determine which portion of the disclosed SEQ ID NO: 1 is in fact coding versus non-coding because it is not described which portion of the full length cDNA SEQ ID NO: 1 represents (i.e. the 5' end, the middle, the 3'end, etc.).

Claim 3 encompasses any nucleic acid of 15 nucleotides or more that specifically hybridizes to a molecule comprising SEQ ID NO: 1. Such a nucleic acid encompasses full length cDNA, genomic DNA, variants of many forms, nucleic acids from other species of animals, etc.

Claims 4-9 are method claims which utilize DNA that hybridizes to SEQ ID NO: 1 (claim 4) or the DNA of claim 3 (claims 6-10).

The large genus of nucleic acids encompassed by the claims is represented in the specification by a nucleic acid consisting of instant SEQ ID NO: 1. Thus, applicant has express possession of only one species in a genus which comprises many, many different possibilities. The present claims encompass full-length genes and cDNAs that are not fully described, other than that they contain or hybridize to instant SEQ ID NO: 1 which is a partial cDNA. There is substantial variability among the species of nucleic acid molecules encompassed within the scope of the claims because SEQ ID NO: 1 is only a fragment of any full-length gene or cDNA species. The partial cDNA provided herein does not include a disclosure of an open reading frame of which it is a part is not representative of the genus of cDNAs and genes encompassed by the claims because no information regarding the coding capacity of the any cDNA molecule

is disclosed. Since the claimed genus encompasses genes yet to be discovered, the disclosed structural feature does not constitute a substantial portion of the claimed genus.

With regard to the written description, all of these claims encompass nucleic acid sequences or methods which utilize nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 3-9 include modifications allowed by the hybridization language for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only a nucleic acid consisting of instant SEQ ID NO: 1 and nucleic acids consisting of fragments of instant SEQ ID NO: 1 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

Weighing all factors, including the partial structure of the DNAs that comprise or hybridize to SEQ ID NO: 1, the breadth of the claims as reading on any number of undescribed nucleic acids, and the lack of correlation between the structure and function of the genes and cDNAs that are not described, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of DNAs which comprise SEQ ID NO: 1 or which hybridize to SEQ ID NO: 1, as encompassed by and/or used in the instant product and method claims.

7. Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for testing for an allergic disease, wherein the allergic disease is a cedar pollen allergy via the detection of SEQ ID NO: 1 within a sample suing the methods set forth in the claims, does not reasonably provide enablement for methods for the detection of any allergic disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of the Invention and Breadth of the Claims

The invention provides a method for testing for allergic disease which utilizes the detection of a differentially expressed cDNA molecule in a sample of RNA isolated from T cells. The rejected claims encompass the detection of any allergic disease, including pet allergies, food allergies, dust mite allergies, allergies to any type of pollen, etc.

Guidance in the Specification and Working Examples

The specification teaches that instant SEQ ID NO: 1 is differentially expressed in patients that suffer from cedar pollen allergy as compared to those that do not (Example 6, p. 20). The specification demonstrates that a significantly higher level of SEQ ID NO: 1 expression was seen in an group of cedar pollen allergy sufferers (high IgE group) when compared to a control group (Table 5 and Fig. 2). In order to demonstrate that the allergy reaction being tested is indeed cedar pollen reaction, the specification uses as control variables for comparison cypress pollen and two types of house dust mites (Table 2). The specification does not provide any additional guidance as to other allergies, other than cedar pollen allergy, that might be associated with differential expression of instant SEQ ID NO: 1.

State of the Art

Instant SEQ ID NO: 1 is a novel sequence. The prior art does not provide any guidance as to other types of allergies that may be indicated by increased expression of instant SEQ ID NO: 1. The prior art does not provide any teaching that suggests that instant SEQ ID NO: 1 is a "universal" indicator of allergic disease.

Skill in the Art and Unpredictability, and, Quantity of Experiment

While the level of skill in the relevant art is quite high, the unpredictability with regard to the instantly claimed invention is higher. It is entirely unpredictable which other types of allergies might be tested for using an assay for the detection of expression of SEQ ID NO: 1, in light of the fact that there are a wide variety of possible allergens known. This is especially highlighted by the instant specification which uses two other dust mite allergens and a different pollen allergen as controls in the experiments for establishing the utility of instant SEQ ID NO: 1 as an indicator of cedar pollen allergy. The practice of the claimed invention commensurate in scope with the broad claims would require an extremely large amount of experimentation wherein hundreds of thousands of patients with different types of allergies are screened and tested to determine whether or not instant SEQ ID NO: 1 is in fact a marker for types of allergic disease other than cedar pollen allergy.

Conclusion

Thus, having carefully considered each of these factors, it is concluded that it would require undue experimentation to make and use the claimed invention commensurate in scope with the instant claims which are directed towards testing for any possible allergic disease.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, and 3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Because the claims read on nucleic acid molecules that would occur in nature (for example an mRNA molecule), untouched by the hand of man, these claims, as broadly drawn, encompass non-statutory subject matter. This rejection may be overcome by amendment of the claims to include, for example, language clarifying that the claimed nucleic acids are intended to be isolated and/or purified nucleic acids.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 4-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite because it recites a preamble that sets forth a method for detecting the nucleic acid of claim 1 (a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1), but the single method step requires only that the method "uses DNA that hybridizes to SEQ ID NO: 1." Thus, it is not clear from the recitation of the claim how or if the preamble breathes life and meaning into the claim. It is not clear if applicant intends to claim any method that uses a DNA that hybridizes to SEQ ID NO: 1, and therefore any method that utilizes a DNA a that would hybridize to SEQ ID NO: 1 under any stringency conditions would be encompassed

within the claim, or if applicant intends to claim a method wherein SEQ ID NO: 1 is positively detected (for which no method step exists in the instant claim). Clarification is required.

Claims 5-9 are indefinite because it is not clear how the purpose of the method as recited in the preamble is accomplished by completing the recited steps. Claims 5-9 are drawn to a method for testing for an allergic disease, yet the claims recite a final step of measuring the amount of an RNA (claims 5, 8, and 9) or comparing the amount of a DNA amplified (claims 6 and 7). The claims do not set forth the relationship between the measuring or comparing and the testing for allergic disease and therefore, it is not clear whether the claims are intended to be drawn to a method for testing for allergic disease or a method for measuring or comparing nucleic acids. Clarification is required.

Claims 5-9 are further indefinite over the recitation "a control (normal group)" as recited in step (d) of claim 5 and step (e) of claim 6. This recitation is indefinite because it is not clear if applicant intends to be limiting the control such that it must be a "normal group" or if applicant is simply setting forth that the control is also referred to as a "normal group." Further, it is not clear what would be meant by a "normal group" because "normal" is a relative term for which no basis for judgment is given.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 3 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Baumgartner *et al.* (US 5792850).

Baumgartner *et al.* teach a DNA that specifically hybridizes to the a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 and that is at least 15 nucleotides long. Specifically, Baumgartner *et al.* teach their instant SEQ ID NO: 12 which is a 23 base pair primer that is identical to nucleotides 1-23 of instant SEQ ID NO: 1. This primer would be expected to specifically hybridize to instant SEQ ID NO: 1. The specification defines "specifically hybridizes" on page 9 as meaning "that under normal hybridization conditions, preferably stringent conditions, there is no significant cross hybridization with DAN and/or RNA encoding other genes (lines 19-21)." The nucleic acid taught by Baumgartner *et al.* is considered to meet this definition, because this definition is entirely context dependent upon the sample being assayed, and thus, in some samples, the sequence taught by Baumgartner *et al.* would certainly be expected to meet the limitations of the definition. Further, it is noted that the nucleic acid taught by Baumgartner *et al.* appears to be substantially identical to the claimed nucleic acid as it meets all of the structural limitations of claim 3.

Further, Baumgartner *et al.* teach a method which uses a DNA that hybridizes to SEQ ID NO: 1 (Example 2, Col. 18). Specifically, Baumgartner *et al.* teach an amplification method which uses their SEQ ID NO: 12 as a primer. This method is considered to read on claim 4 insofar as it performs the single method step required by claim 4, that is it uses a DNA that hybridizes to SEQ ID NO: 1. As discussed in the 112 2nd rejection, it is not clear how or if the preamble of the claim breathes life into the claim, therefore, even though Baumgartner *et al.* do

not specifically recite the detection of SEQ ID NO: 1 the method taught therein is considered to meet the limitations of claim 4.

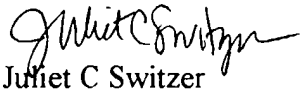
Conclusion

13. A nucleic acid consisting of instant SEQ ID NO: 1 is free of the prior art. Further, the prior art does not teach or suggest that instant SEQ ID NO: 1 is differentially expressed in T-cells in response to cedar pollen allergy.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Juliet C Switzer
Examiner
Art Unit 1634

October 30, 2003